REMARKS

The Official Action dated February 21, 2008 and the references cited therein have been carefully reviewed. In view of the amendments submitted herewith and the following remarks, favorable reconsideration and allowance of this application are respectfully requested.

This paper is being submitted with a request for continued examination. It is noted that a shortened statutory response period of three (3) months was set forth in the February 21, 2008 Official Action. This response is being filed with a petition for a three month extension of time and the requisite fees.

At the outset, Applicants note that the Examiner has indicated that claims 23-26 are directed to allowable subject matter.

The Examiner continues to maintain that the specification incorporates essential material by reference because the genes listed in Table S6 are not accompanied by SEQ ID NOs. Applicants again strenuously disagree with the Examiner as the skilled person is readily able to obtain the requisite information from a variety of sources, e.g., research articles in the public domain, and on the web at the Unigene and GenBank websites. The skilled person in molecular diagnostics readily avails himself to such resources and thus the sequence information encompasses material "that is well known in the art", which patent applications preferably omit. In order to expedite prosecution however, a sequence listing of the sequences obtainable from the Unigene website is being submitted with this response in both paper copy and computer readable forms. The undersigned respectfully requests entry of the sequence listing into the application and verifies that the paper copy and CRF forms are identical and do not introduce new matter into the application.

Claims 2, 13, 14, 17, and 24 stand rejected under 35 U.S.C. 112, second paragraph as allegedly indefinite for referring to Table S6.

The Examiner has rejected claims 1, 2, 5-11, and 27 under 35 U.S.C. 112, first paragraph as allegedly failing to satisfy the written description requirements of the statute.

Claims 16-20 and 22 remain rejected under 35 U.S. C. 102(e) as allegedly anticipated by the disclosure in US Patent Application 2004/0018525 to Wirtz et al.

At page 18 of the Official Action, the Examiner has rejected claims 12-14 under 35 U.S.C. as failing to comply with the enablement requirement.

The foregoing objections and rejections constitute all of the grounds set forth in the February 21, 2008 Official Action for refusing the present application. Each of these objections and rejections are traversed for the reasons set forth below.

THE SPECIFICATION AS AMENDED FULLY COMPLIES WITH THE REQUIREMENTS OF THE PATENT STATUTES

As set forth in Applicant's previous response, incorporating sequence identifiers into the specification and Table S6 in particular is not necessary for the skilled artisan to practice the invention as claimed. Indeed, a person skilled in the art of molecular diagnosis readily avails himself to the sequence information obtainable on the web to facilitate planning of experiments and verifying experimental results.

In order to comply with the Examiner's requirement, each of the Unigene numbers was accessed on the Unigene website. As shown for Hs.28914, adenine phosphoribosyltransferase the provided Unigene number is entered into the search bar. See Exhibit I. The search result is selected and the data presented in Exhibit 2 is accessed. As can be seen at page 2 of Exhibit 2, 7 human mRNA sequences are listed by GenBank accession number. Each of these sequences were then accessed through the GenBank hyperlink. See Exhibit 3. On Exhibit 3

under Sequence Information, the NM_000485.2, link is selected and one obtains access to the sequence information (Exhibit 4) relating to Hs.28914. To ensure that the sequences included in the sequence listing were publically available as of the priority date, GenBank provides the "Reports" link next to the accession number on Exhibit 4. Selecting "Reports" provides the revision history and indicates when the sequences were deposited and updated (if any updates were made). See Exhibit 5. The differences between the sequences are shown by comparing the current sequence information with earlier deposited sequence information. In the case of adenine phosphoribotransferase, the current version is a longer form of isoform which was available on the web as of September 6, 2003. See Exhibit 6. Only a single sequence for APRT was listed before the priority date and this sequence has been designated as SEQ ID NO: 1. All of the sequences selected for the sequence listing were in the public domain before October 3, 2003, the priority date of the instant application. If the sequence listed in GenBank was not deposited as of this date, it was not included in the sequence listing.

In certain instances as in Hs.154443, MCM4, the Unigene number listed in Table S6 had been retired. See Exhibit 7. The Unigene website indicates that entries can be retired for the following reasons:

Why are some UniGene clusters retired?

UniGene clusters can eventually be "retired" for various reasons, such as:

- the sequences in a cluster might be retracted by the submitters because they are found to have contaminants.
- two clusters can be joined, in which case one of the original cluster IDs would be retired.
- a cluster can be split into two or more clusters in such a way that none of the smaller clusters can be recognized to be "the same as" the original cluster.

Nonetheless in these instances, selection of the retired number provides access to the new entry number. For MCM4, this number is Hs.460184. See Exhibit 8. This new number is then selected, the sequence information as shown Exhibit 9 is

obtained, which is comparable to data from Exhibit 2 above, and the process is repeated as set forth above. The sequences listed are searched in GenBank as above to ensure they were in the public domain as of the priority date. Those sequences were then included in the sequence listing. For MCM4, 4 human mRNA sequences were available in the public domain as of the priority date and these are designated as SEQ ID NOS: 2-5.

All of the sequence listed in the sequence listing are available in GenBank under the names listed in Table S6 and were publically available when the application was filed.

It is submitted that the inclusion of sequence identifiers in the present application and claims renders the objection/rejection to the specification moot. Applicants therefore request that this rejection be withdrawn.

THE METES AND BOUNDS OF CLAIMS 2, 13, 14, 17 AND 24 ARE CLEAR TO ONE OF ORDINARY SKILL IN THE ART

The Examiner has rejected the aforementioned claims as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter regarded as the invention. While continuing to disagree with the Examiner, the claims have been amended to make reference to the sequence identifiers set forth in amended Table S6. It is submitted that this amendment removes any perceived ambiguity from the claims. Accordingly, Applicants request that the rejection be withdrawn.

THE SPECIFICATION FULLY ENABLES THE PRACTICE OF THE SUBJECT MATTER ENCOMPASSED BY CLAIMS 1, 2, 5-11 AND 27 AS AMENDED

Claims 1, 2, 5-11 and 27 stand rejected under 35 U.S.C. §112, first paragraph as allegedly lacking enablement. Claim 1 and claims dependent therefrom now require comparison of the expression profile of nucleic acids isolated from the patient to a previously determined signature expression profile which is associated with low or high NPI, higher NPI levels being correlated with a poorer prognosis. See page 12, last full

paragraph. As set forth at page 40, in the description of Figure 2, the present inventor has identified an Expression signature which correlates with NPI. Also see page 49 for a description. It is respectfully submitted that the amendment to claim 1 eliminates the Examiner's concerns regarding the comparison step as it relates to "comparing to any other level" as stated at page 12 of the Official Action.

Claim 27 has also been amended to include reference to known NPI as well as known prognosis. This amendment more clearly specifies that it is the levels of the expression products from claim 1 that are to be determined relative to previously determined standard levels associated with a particular NPI.

The Examiner states that the specification does not provide any evidence for upregulation as specified in claim 8. Applicants respectfully disagree. Indeed, as set forth at page 5, fourth full paragraph, the last two genes in table S6 are highly expressed in low NPI tumors (the negative genes) whilst the first 60 genes are highly expressed in high NPI tumors. Thus, inasmuch as claim 1 references NPI, Applicants submit that the claims as amended are fully enabled and request that the rejection of the aforementioned claims for lack of enablement be withdrawn.

CLAIMS 16-20 AND 22 ARE NOVEL OVER US 2004/0018525 TO WIRTZ ET AL.

In order for a reference to anticipate a claim, each and every element must be identically disclosed therein. Claim 16 and 22 have been amended to recite that the instant kits comprise no more than 500 binding members for the prognostic set of genes. As acknowledged by the Examiner, Wirtz et al. disclose use of a microarray comprising over 40,000 genes. Inasmuch as the present claims are not identical to the disclosure in Wirtz et al., the rejection of the aforementioned claims under 35 U.S.C. §102(e) is untenable and

should be withdrawn.

CLAIMS 12-14 AS AMENDED ARE FULLY ENABLED BY THE DISCLOSURE IN THE APPLICATION

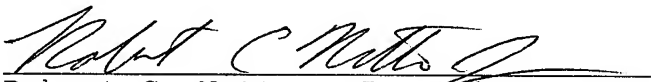
The Examiner has asserted that claims 12-14 are lacking in enablement for not containing reference to the nucleic acids set forth in Table S6 by SEQ ID NOS: The claims have been amended to recite the SEQ ID NOS: in amended table S6, thereby obviating this rejection. Accordingly, Applicants request that the rejection be withdrawn.

CONCLUSION

In view of the remarks presented herewith, it is respectfully urged that the objections and rejections set forth in the February 21, 2008 Official Action be withdrawn and that this application be passed to issue.

In the event the Examiner is not persuaded as to the allowability of any claim, and it appears that any outstanding issues may be resolved through a telephone interview, the Examiner is requested to telephone the undersigned at the phone number given below.

Respectfully submitted,
DANN, DORFMAN, HERRELL AND SKILLMAN
A Professional Corporation

By 
Robert C. Netter, Jr., Ph.D., J.D.
PTO Registration No. 56,422

Telephone: (215) 563-4100
Facsimile: (215) 563-4044
Enclosures: Exhibits
Sequence listing